Amendments to the Specification:

Please replace the paragraph beginning on page 2, line 22, with the following rewritten paragraph:

C_{1-6} alkyl group (wherein the C_{1-6} alkyl group may be arbitrarily substituted with halogen atom, hydroxy group, C_{1-6} alkoxy group (wherein the C_{1-6} alkoxy group may be arbitrarily substituted with halogen atom), C_{6-14} aryl group or C_{2-9} heteroaryl group (wherein each of the C_{6-14} aryl group or C_{2-9} heteroaryl group may be arbitrarily substituted with 1 to 3 R^{10} wherein R^{10} is halogen atom; hydroxy group; C_{1-6} alkyl group (wherein the C_{1-6} alkyl group may be arbitrarily substituted with halogen atom, hydroxy group or C_{1-6} alkoxy group (wherein the C_{1-6} alkoxy group may be arbitrarily substituted with halogen atom)); C_{1-6} alkoxy group (wherein the C_{1-6} alkoxy group may be arbitrarily substituted with halogen atom); nitro group; cyano group; formyl group; formamide group; sulfonylamino group; sulfonyl group; amino group; C_{1-6} alkylamino group; di-C_{1-6} alkylamino group; C_{1-6} alkylcarbonylamino group; C_{1-6} alkylsulfonylamino group; aminocarbonyl group; C_{1-6} alkylaminocarbonyl group; di-C_{1-6} alkylaminocarbonyl group; C_{1-6} alkylcarbonyl group; C_{1-6} alkoxycarbonyl group; aminosulfonyl group; C_{1-6} alkylsulfonyl group; carboxy group or C_{6-14} arylcarbonyl group, and when a plurality of R^{10} are present, they may be identical or different from each other),

~~-~~C_{6-14} aryl group or C_{2-9} heteroaryl group (wherein each of the C_{6-14} aryl group or C_{2-9} heteroaryl group may be arbitrarily substituted with 1 to 3 R^{10} wherein R^{10} has the above-mentioned meaning)~~)~~;

Please replace the paragraph beginning on page 4, line 35, with the following rewritten paragraph:

(5) The benzopyran compound as set forth in (2), wherein R^5 is C_{1-6} alkyl group, C_{3-8} cycloalkyl group or C_{6-14} aryl group;

Please replace the paragraph beginning on page 5, line 2, with the following rewritten paragraph:

(6) The benzopyran compound as set forth in (3), wherein R^5 is C_{1-6} alkyl group, C_{3-8} cycloalkyl group or C_{6-14} aryl group;

Please replace the paragraph beginning on page 5, line 4, with the following rewritten paragraph:

(7) The benzopyran compound as set forth in (4), wherein R^5 is C_{1-6} alkyl group, C_{3-8} cycloalkyl group or C_{6-14} aryl group;

Please replace the paragraph beginning on page 5, line 12, with the following rewritten paragraph:

(10) The benzopyran compound as set forth in (8), wherein R^5 is C_{1-6} alkyl group or C_{6-14} aryl group, R^6 is hydrogen atom or methyl group, Y is SO_2, and Z is C_{1-4} alkyl group;

Please replace the paragraph beginning on page 5, line 15, with the following rewritten paragraph:

(11) The benzopyran compound as set forth in (8), wherein R^5 is C_{1-6} alkyl group or C_{6-14} aryl group, R^6 is hydrogen atom or methyl group, Y is a bond, and Z is C_{1-4} alkyl group;

Please replace the paragraph beginning on page 5, line 33, with the following rewritten paragraph:

(18) A benzopyran compound which is N-{(*3R*, 4S**)-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-benzopyran-7-yl} methanesulfonamide ~~maleate~~;

Please replace the paragraph beginning on page 6, line 1, with the following rewritten paragraph:

(19) A benzopyran compound which is N-{(*3R*, 4S**)-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-benzopyran-7-yl} ethanesulfonamide ~~hydrochloride~~;

Please replace the paragraph beginning on page 6, line 4, with the following rewritten paragraph:

(20) A benzopyran compound which is 1,1,1-trifluoro-N-{(*3R*, 4S**)-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-benzopyran-7-yl}-methanesulfonamide ~~maleate~~;

Please replace the paragraph beginning on page 6, line 7, with the following rewritten paragraph:

(21) A benzopyran compound which is N-{(*3R**, *4S**)-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-benzopyran-7-yl}-N-methylmethanesulfonamide ~~hydrochloride~~;

Please replace the paragraph beginning on page 6, line 13, with the following rewritten paragraph:

(23) A benzopyran compound which is (*3R**, *4S**)-2,2-dimethyl-7-dimethylamino-4-[(2-phenylethyl)amino]-3-chromanol ~~hydrochloride~~;

Please replace the paragraph beginning on page 6, line 15, with the following rewritten paragraph:

(24) A benzopyran compound which is (*3R**, *4S**)-2,2-dimethyl-7-methylamino-4-[(2-phenylethyl)amino]-3-chromanol ~~hydrochloride~~;

Please replace the paragraph beginning on page 6, line 17, with the following rewritten paragraph:

(25) A benzopyran compound which is (*3R**, *4S**)-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2-dimethyl-7-dimethylamino-3-chromanol ~~hydrochloride~~;

Please replace the paragraph beginning on page 6, line 21, with the following rewritten paragraph:

(27) A benzopyran compound which is (*3R*, 4S**)-6-methoxy-2,2-dimethyl-7-methylamino-4-[(2-phenylethyl)amino]-3-chromanol ~~hydrochloride~~;

Please replace the paragraph beginning on page 6, line 29, with the following rewritten paragraph:

(30) A benzopyran compound which is (*3R*, 4S**)-2,2-dimethyl-7-methylethylamino-4-[(2-phenylethyl)amino]-3-chromanol ~~hydrochloride~~.

Please replace the paragraph beginning on page 6, line 31, with the following rewritten paragraph:

(31) A benzopyran compound which is N-{(*3R*, 4S**)-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-chromen-7-yl}-N-isopropylmethanesulfonamide ~~hydrochloride~~.

Please replace the paragraph beginning on page 7, line 20, with the following rewritten paragraph:

Examples of C_{1-6} alkyl group are such as methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, 1-pentyl, 2-pentyl, 3-pentyl, i-pentyl, neopentyl, ~~2-2-dimethylpropyl,~~ 1-hexyl, 2-hexyl, 3-hexyl, ~~1-methyl-n-pentyl,~~ 1,1,2-trimethyl-n-propyl, 1,2,2-trimethyl-n-propyl, 3,3-dimethyl-n-butyl and the like.

Please replace the paragraph beginning on page 7, line 28, with the following rewritten paragraph:

Examples of C_{1-6} alkoxy group are such as methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, i-butoxy, s-butoxy, t-butoxy, 1-pentyloxy, 2-pentyloxy, 3-pentyloxy, i-pentyloxy, neopentyloxy, ~~2-2-dimethylpropoxy,~~ 1-hexyloxy, 2-hexyloxy, 3-hexyloxy, ~~1-methyl-n-pentyloxy,~~ 1, 1, 2-trimethyl-n-propoxy, 1, 2, 2-trimethyl-n-propoxy, 3, 3-dimethyl-n-butoxy and the like.

Please replace the paragraph beginning on page 9, line 21, with the following rewritten paragraph:

Examples of C_{1-6} alkylamino group are such as methylamino, ethylamino, n-propylamino, i-propylamino, c-propylamino, n-butylamino, i-butylamino, s-butylamino, t-butylamino, c-butylamino, 1-pentylamino, 2-pentylamino, 3-pentylamino, i-pentylamino, neopentylamino, t-pentylamino, c-pentylamino, 1-hexylamino, 2-hexylamino, 3-hexylamino, c-hexylamino, ~~1-methyl-n-pentylamine,~~ 1,1,2-trimethyl-n-propylamino, 1,2,2-trimethyl-n-propylamino, 3,3-dimethyl-n-butylamino and the like.

Please replace the paragraph beginning on page 12, line 3, with the following rewritten paragraph:

Examples of C_{6-14} arylcarbonyl group are such as benzoyl, p-methylbenzoyl, p-t-butylbenzoyl, p-methoxybenzoyl, p-chlorobenzoyl, p-nitrobenzoyl, p-cyanobenzoyl, o-biphenylylcarbonyl, m-biphenylylcarbonyl, p-biphenylylcarbonyl, □-naphthylcarbonyl, □-naphthylcarbonyl, 1-anthrylcarbonyl, 2-anthrylcarbonyl, 9-anthrylcarbonyl, 1-phenanthrylcarbonyl, 2-phenanthrylcarbonyl, 3-phenanthrylcarbonyl, 4-phenanthrylcarbonyl, 9-phenanthrylcarbonyl and the like.

Please replace the paragraph beginning on page 12, line 10, with the following rewritten paragraph:

Examples of C_{1-6} alkylureylene group are such as methylureylene, ethylureylene, n-propylureylene, i-propylureylene, n-butylureylene, i-butylureylene, s-butylureylene, t-butylureylene, 1-pentylureylene, 2-pentylureylene, 3-pentylureylene, i-pentylureylene, neopentylureylene, ~~2, 2 dimethylpropylureylene,~~ 1-hexylureylene, 2-hexylureylene, 3-hexylureylene, ~~1 methyl n pentylureylene,~~ 1,1,2-trimethyl-n-pentylureylene, 1,2,2-trimethyl-n-pentylureylene, 3,3-dimethyl-n-butylureylene and the like.

Please replace the paragraph beginning on page 12 line 33, with the following rewritten paragraph:

Examples of C_{6-14} arylcarbonylamino group are such as benzoylamino, p-methylbenzoylamino, p-t-butylbenzoylamino, p-methoxybenzoylamino, p-chlorobenzoylamino, p-nitrobenzoylamino, p-cyanobenzoylamino, o-biphenylylcarbonylamino, m-biphenylylcarbonylamino, p-biphenylylcarbonylamino, α-naphthylcarbonylamino, ß-naphthylcarbonylamino, 1-anthrylcarbonylamino, 2-anthrylcarbonylamino, 9-anthrylcarbonylamino, 1-phenanthrylcarbonylamino, 2-phenanthrylcarbonylamino, 3-phenanthrylcarbonylamino, 4-phenanthrylcarbonylamino, 9-phenanthrylcarbonylamino and the like.

Please replace the paragraph beginning on page 13, line 9, with the following rewritten paragraph:

Examples of C_{3-8} cycloalkenyl group are such as 1-c-pentenyl, 2-c-pentenyl, 3-c-pentenyl, 1-methyl-2-c-pentenyl, 1-methyl-3-c-pentenyl, 2-methyl-1-c-pentenyl, 2-methyl-2-c-pentenyl, 2-methyl-3-c-pentenyl, 2-methyl-4-c-pentenyl, 2-methyl-5-c-pentenyl, 2-methylene-c-pentyl, 3-methyl-1-c-pentenyl, 3-methyl-2-c-pentenyl, 3-methyl-3-c-pentenyl, 3-methyl-4-c-pentenyl, 3-methyl-5-c-pentenyl, 3-methylene-c-pentyl, 1-c-hexenyl, 2-c-hexenyl, 3-c-hexenyl, 1-c-heptenynyl, 2-c-heptenynyl, 3-c-heptenynyl, 4-c-heptenynyl, 1-c-octenynyl, 2-c-octenynyl, 3-c-octenynyl, 4-c-octenynyl and the like.

Please replace the paragraph beginning on page 13, line 33, with the following rewritten paragraph:

More preferably, concrete examples of W are hydrogen atom, bromine atom, hydroxy group, methoxy and $NHSO_2Me$ at 6-position, and hydrogen atom and methyl at 8-position, and further preferably hydrogen atom, hydroxy group and methoxy at 6-position.

Please replace the paragraph beginning on page 79, line 31, with the following rewritten paragraph:

Sulfoxide type solvents exemplified by dimethylsulfoxide; amide type solvents exemplified by dimethylformamide or dimethylacetamide; ether type solvents exemplified by diethyl ether, dimethoxyethane, tetrahydrofuran or cyclopentyl methyl ether; halogen type solvents exemplified by dichloromethane, chloroform ~~and~~ or dichloroethane; nitrile type solvents exemplified by acetonitrile ~~and~~ or propionitrile; ketone type solvents exemplified by acetone, methyl ethyl ketone ~~and~~ or methyl isobutyl ketone; aromatic hydrocarbon type solvents exemplified by benzene and toluene; hydrocarbon type solvents exemplified by hexane ~~and~~ or heptane; and ester type solvents exemplified by ethyl acetate may be mentioned. Further, the reaction can be carried out in the absence of any solvent. Preferably, ether type solvents may be mentioned.

Please replace the paragraph beginning on page 80, line 11, with the following rewritten paragraph:

The base includes trialkylamines exemplified by triethylamine and ethyldiisopropylamine; pyridine amines exemplified by pyridine, 2,6-lutidine, 2,6-di-t-butylpyridine, 2,6-di-t-butyl-4-methylpyridine and proton ~~pomp~~sponge; and inorganic bases exemplified by sodium hydroxide, potassium hydroxide and potassium carbonate. Preferably, triethylamine, ethyldiisopropylamine and pyridine may be mentioned.

Please replace the paragraph beginning on page 80, line 34, with the following rewritten paragraph:

The base includes trialkylamines exemplified by triethylamine and ethyldiisopropylamine; pyridine amines exemplified by pyridine, 2,6-lutidine, 2,6-di-t-butylpyridine, 2,6-di-t-butyl-4-methylpyridine and proton ~~pomp~~sponge; and inorganic bases exemplified by sodium hydroxide, potassium hydroxide and potassium carbonate. Preferably, inorganic bases exemplified by potassium carbonate may be mentioned.

Please replace the paragraph beginning on page 81, line 33, with the following rewritten paragraph:

In addition, compound (~~I-2~~I-4) wherein R^6 is C_{1-4} alkyl group can be obtained by reacting compound (I-3) with R^6-X^2 in the presence of a base.

Please replace the paragraph beginning on page 84, line 26, with the following rewritten paragraph:

The base includes trialkylamines exemplified by triethylamine and ethyldiisopropylamine; pyridine amines exemplified by pyridine, 2,6-lutidine, 2,6-di-t-butylpyridine, 2,6-di-t-butyl-4-methylpyridine and proton ~~pomp~~sponge; metal alkoxides exemplified by ~~potassium t-butoxide~~potassium t-butoxide, ~~sodium t-butoxide~~sodium t-butoxide, sodium ethoxide and potassium ethoxide and inorganic bases exemplified by sodium hydroxide, potassium hydroxide, potassium carbonate, sodium carbonate, potassium hydrogen carbonate and sodium hydrogen carbonate. Preferably, metal alkoxides and inorganic bases may be mentioned.

Please replace the paragraph beginning on page 85, line 12, with the following rewritten paragraph:

The deprotection is achieved by treating according to any known process, such as by treatment with an acid or a base, or by ~~hydrolysis~~hydrogenolysis, or the like.

Please replace the paragraph beginning on page 87, line 23, with the following rewritten paragraph:

Injections, solutions, emulsions, suspensions, syrups and aerosols are prepared by using solvents for the active components such as water, ethyl alcohol, isopropyl alcohol, propylene glycol, 1,3-butylene glycol and polyethylene glycol; surfactants such as sorbitan fatty acid ester, polyoxyethylene sorbitan fatty acid ester, polyoxyethylene fatty acid ester, polyoxyethylene ether of hydrogenated castor oil and lecithin; suspending agents such as carboxymethyl cellulose sodium salt, cellulose derivatives such as methyl cellulose or the like, and natural rubbers such as gum arabic, tragacanth or the like; and preserves such as p-hydroxybenzoic acid esters, benzalkonium chloride, sorbic acid salts and the like.

Please replace the paragraph beginning on page 88, line 20, with the following rewritten paragraph:

Synthesis Example 1

N-{(*3R**, *4S**)-3-~~hydroxy~~Hydroxy-6-methoxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-7-yl} methanesulfonamide

Please replace the paragraph beginning on page 88, line 29, with the following rewritten paragraph:

4-(1,1-dimethyl-2-~~propenyloxy~~propynyloxy)anisole

Please replace the paragraph beginning on page 88, line 33, with the following rewritten paragraph:

To a solution of 4-methoxyphenol (15.0 g, 121 mmol) in acetonitrile (75 mL), 1,8-diazabicyclo[5.4.0]undecene (23.9 g, 157 mmol) was added under ice cooling and the resulting mixture was stirred at 0°C for 30 minutes (Solution 1). To a solution of 2-methyl-3-~~buten~~butyn-2-ol (11.7 g, 139 mmol) in acetonitrile (75 mL), 1,8-diazabicyclo[5.4.0]undecene (23.9 g, 157 mmol) was added under ice cooling, the resulting mixture was stirred at 0°C for 30 minutes, then trifluoroacetic anhydride (25.4 g, 121 mmol) was added and the resulting mixture was stirred at 0°C for 30 minutes (Solution 2). Copper (I) chloride (36 mg, 0.36 mmol) was added to Solution 1, and then Solution 2 was added dropwise thereto over 15 minutes. Upon the conclusion of dropwise addition, the temperature was raised to room temperature, and the mixture was stirred overnight. Upon the completion of the reaction, an aqueous solution of ammonium chloride was added to the reaction solution, and the solvent was distilled off under a reduced pressure. An aqueous solution of 1 mol/L hydrochloric acid was added to the residue, the resulting mixture was extracted with ethyl acetate, the organic phase was washed once with an aqueous solution of 1 mol/L hydrochloric acid, twice with an aqueous solution of saturated sodium hydrogen carbonate and once with saturated sodium chloride solution. Then, the organic phase was dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was directly used for the subsequent reaction.

Please replace the paragraph beginning on page 89, line 22, with the following rewritten paragraph:

A solution of 4-(1,1-dimethyl-2-~~propenyloxy~~propynyloxy)anisole in 1,2-dichlorobenzene (50 mL) was stirred at 190°C for 2 hours. Upon the completion of the reaction, the solvent was distilled off under a reduced pressure. The residue was purified by column chromatography (hexane/chloroform = 3/1) and the aimed product was obtained as red oily substance (2-step, yield: 61%).

Please replace the paragraph beginning on page 90, line 15, with the following rewritten paragraph:

(*3R**, *4R**)-3,4-~~epoxy~~Epoxy-6-methoxy-2, 2-dimethyl-7-nitro-3,4-dihydro-2H-1-benzopyran

Please replace the paragraph beginning on page 90, line 19, with the following rewritten paragraph:

To a solution (300 mL) of acetonitrile containing 6-methoxy-2,2-dimethyl-7-nitro-2H-1-benzopyran (10.0 g, 42.5 mmol), N-methyl imidazole (0.678 mL, 8.50 mmol), (R,R,S,S)-Ph,Ph salen manganese complex (XY) (880 mg, 0.850 mmol) and iodosobenzene (18.7 mg, 85.0 mmol) were added at room temperature and the mixture was stirred for 2 hours. Upon the completion of the reaction, an aqueous solution of sodium thiosulfate was added to the reaction solution, the resulting solution was filtered through celite. The resulting filtrate extracted with ethyl acetate. The organic phase was washed with water and sodium chloride solution, and then dried over anhydrous magnesium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 4/1) and the aimed product was obtained as yellow ~~crystal~~ crystals (yield: 75%, optical purity: 99.7% ee).

Please replace the paragraph beginning on page 91, line 2, with the following rewritten paragraph:

(*3R**, *4S**)-6-~~methoxy~~Methoxy-2, 2-dimethyl-7-nitro-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-3-ol

Please replace the paragraph beginning on page 91, line 9, with the following rewritten paragraph:

To a solution of (*3R**, ~~*4S*~~*4R**)-3,4-epoxy-6-methoxy-2, 2-dimethyl-7-nitro-3,4-dihydro-2H-1-benzopyran (2.50 g, 9.95 mmol) in 1,4-dioxane (5.0 mL), lithium perchlorate (1.06 g, 9.95 mmol) and 4~~2~~-(phenylethyl)amine (1.50 mL, 11.9 mmol) were added at room temperature and the mixture was stirred at 80 °C for 1 hour. Upon the completion of the reaction, an aqueous solution of saturated ammonium chloride was added to the reaction solution, and the resulting solution was extracted with ethyl acetate. The organic phase was washed with saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 6/4) and the aimed product was obtained as orange amorphous substance (quantitative yield).

Please replace the paragraph beginning on page 91, line 31, with the following rewritten paragraph:

To a solution of (*3R**, *4S**)-6-methoxy-2, 2-dimethyl-7-nitro-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-3-ol (407 mg, 1.09 mmol) and di-t-butyl di~~-~~carbonate (477 mg, 2.19 mmol) in tetrahydrofuran (6.0 mL), triethylamine (305 mL, 2.19 mmol) was added at 0 °C and the mixture was stirred at room temperature overnight. Upon the completion of the reaction, an aqueous solution of saturated sodium carbonate was added to the reaction solution, and the resulting solution was extracted with ethyl acetate. The organic phase was washed with 1 mol/L hydrochloric acid aqueous solution and saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 4/1) and the aimed product was obtained as yellow amorphous substance (yield: 88%).

Please replace the paragraph beginning on page 92, line 32, with the following rewritten paragraph:

To a solution of t-butyl (2-phenylethyl) (*3R**, *4S**)-7-amino-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2H-1-benzopyran-4-yl carbamate (1.16 ~~mgg~~, 2.62 mmol) in pyridine (11.6 mL), methanesulfonyl chloride (0.223 mL, 2.88 mmol) was added at 0°C, the temperature was raised to room temperature and the resulting mixture was stirred at room temperature overnight. Upon the completion of the reaction, an aqueous solution (ca. 30 mL) of 1 mol/L hydrochloric acid was added to the reaction solution to adjust pH to 5-9, and then the mixture was extracted with ethyl acetate. The organic phase was washed with saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 3/1) and the aimed product was obtained as colorless oily substance (yield: 77%).

Please replace the paragraph beginning on page 93, line 10, with the following rewritten paragraph:

N-{(*3R**, *4S**)-3-~~hydroxy~~Hydroxy-6-methoxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-7-yl} methanesulfonamide

Please replace the paragraph beginning on page 93, line 17, with the following rewritten paragraph:

A solution of t-butyl (2-phenylethyl) (*3R**, *4S**)-3-hydroxy-6-methoxy-2,2-dimethyl-7-[(methylsulfonyl)amino]-3,4-dihydro-2H-1-benzopyran-4-yl carbamate (300 mg, 0.577 mmol) in dichloromethane (3.0 mL) was cooled to 0 °C, trifluoroacetic acid (3.0 mL) was added thereto, and the resulting mixture was stirred at 0 °C for 1 hour. Upon the completion of the reaction, the solvent was distilled off, and the residue was purified by column chromatography (hexane/ethyl acetate = 2/1) and the aimed product was obtained as gray amorphous substance (yield: 99%).

Please replace the paragraph beginning on page 93, line 28, with the following rewritten paragraph:

Synthesis Example 2

N-{(*3R**, *4S**)-3,6-~~dihydroxy~~Dihydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-7-yl} methanesulfonamide

Please replace the paragraph beginning on page 94, line 1, with the following rewritten paragraph:

To a solution of t-butyl (2-phenylethyl) (*3R**, *4S**)-7-{(methylsulfonyl)amino}-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2H-1-benzopyran-4-yl carbamate (300 mg, 0.58 mmol) in dichloromethane (3.0 mL), a solution ~~(2.88 mL, 2.88 mmol)~~ of 1 mol/L boron tribromide-dichloromethane (2.88 mL, 2.88 mmol) was added under cooling with ice and the resulting mixture was stirred at 0 °C for 1 hour. Upon the completion of the reaction, methanol was added and the resulting mixture was stirred for 30 minutes, and the solvent was distilled off. The residue was washed ethyl acetate, and the resulting solid was dried under a reduced pressure at 50 °C for 2 hours, and thereby hydrobromide of the aimed product was obtained as yellow solid (yield: 56%).

Please replace the paragraph beginning on page 94, line 16, with the following rewritten paragraph:

Synthesis Example 3

N-{(*3R**, *4S**)-3-~~hydroxy~~Hydroxy-6-methoxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-7-yl}-N-methylmethanesulfonamide

Please replace the paragraph beginning on page 95, line 9, with the following rewritten paragraph:

N-{(*3R**, *4S**)-3-~~hydroxy~~Hydroxy-6-methoxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-7-yl}-N-methyl-methanesulfonamide

Please replace the paragraph beginning on page 95, line 16, with the following rewritten paragraph:

A solution of 4 mol/L hydrogen ~~chloride 1~~chloride in 1,4-dioxane (2.01 mL, 8.04 mmol) was added to t-butyl (2-phenylethyl) (*3R**, *4S**)-3-hydroxy-6-methoxy-2,2-dimethyl-7-(N-methyl-N- methylsulfonylamino)-3,4-dihydro-2H-1-benzopyran-4-yl carbamate (201 mg, 0.389 mmol) at room temperature, and the resulting mixture was stirred at 100 °C for 30 minutes. Upon the completion of the reaction, the solvent was distilled off. The resulting solid was washed with 2-propanol and thereby hydrochloride of the aimed product was obtained as pale blue solid (yield: 84%).

Please replace the paragraph beginning on page 95, line 29, with the following rewritten paragraph:

Synthesis Example 4

N-{(*3R**, *4S**)-4-[(2-~~cyclohexylethyl~~Cyclohexylethyl)amino]-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2H-1-benzopyran-7-yl} methanesulfonamide

Please replace the paragraph beginning on page 96, line 6, with the following rewritten paragraph:

(*3R**, *4S**)-4-~~amino~~Amino-6-methoxy-2,2-dimethyl-7-nitro-3,4-dihydro-2H-1-benzopyran-3-ol

Please replace the paragraph beginning on page 96, line 11, with the following rewritten paragraph:

To a solution of (*3R**, *4R**)-3,4-epoxy-6-methoxy-2,2-dimethyl-7-nitro-3,4-dihydro-2H-1-benzopyran (2.64 g, 10.5 mmol) in ethanol (26 mL), an ~~ammonium~~ ammonia water (26 mL) was added, and the resulting mixture was stirred in a sealed tube at 100 °C for 2 hours. Upon the completion of the reaction, the solvent was distilled off. An aqueous solution of saturated sodium carbonate was added to the residue, and the resulting mixture was extracted with ethyl acetate. The organic phase was washed with saturated sodium chloride solution, dried over anhydrous magnesium sulfate and thereby the aimed product was obtained as red amorphous substance (yield: 84%).

Please replace the paragraph beginning on page 96, line 29, with the following rewritten paragraph:

To a solution of (*3R**, *4S**)-4-amino-6-methoxy-2, 2-dimethyl-7-nitro-3,4-dihydro-2H-1-benzopyran-3-ol (2.62 g, 9.77 mmol) and di-t-butyl di-carbonate (4.26 g, 19.5 mmol) in tetrahydrofuran (52 mL), triethylamine (2.72 mL, 19.5 mmol) was added at 0 °C and the mixture was stirred at room temperature overnight. Upon the completion of the reaction, an aqueous solution of saturated sodium carbonate was added to the reaction solution, and the resulting solution was extracted with ethyl acetate. The organic phase was washed with 1 mol/L hydrochloric acid aqueous solution and saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 2/1) and the aimed product was obtained as yellow solid (yield: 92%).

Please replace the paragraph beginning on page 98, line 14, with the following rewritten paragraph:

N-{(*3R**, *4S**)- (4-~~amino~~Amino-3-hydroxy-6-~~mehoxy~~methoxy-2,2-dimethyl-3,4-dihydro-2H-1-benzopyran-7-yl)} methanesulfonamide hydrochloride

Please replace the paragraph beginning on page 98, line 21, with the following rewritten paragraph:

A solution of 4 mol/L hydrogen chloride-1,4-dioxane (2.52 mL, ~~10.0~~10.1 mmol) was added to t-butyl {(*3R**, *4S**)-3-hydroxy-6-methoxy-2,2-dimethyl-7-[(methylsulfonyl)amino]-3,4-dihydro-2H-1-benzopyran-4-yl} carbamate (419 mg, 1.00 mmol) at room temperature, and the resulting mixture was stirred at 100 °C for 30 minutes. Upon the completion of the reaction, the solvent was distilled off. The resulting solid was washed with diisopropyl ether and thereby hydrochloride of the aimed product was obtained as colorless solid (yield: 99%).

Please replace the paragraph beginning on page 98, line 30, with the following rewritten paragraph:

N-{(*3R**, *4S**)-4-[(2-~~cyclohexylethyl~~Cyclohexylethyl)amino]-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2H-1-benzopyran-7-yl} methanesulfonamide

Please replace the paragraph beginning on page 99, line 6, with the following rewritten paragraph:

To a solution of N-((3R*, 4S*) 4-amino-3-hydroxy-6-~~mehoxy~~methoxy-2,2-dimethyl-3,4-dihydro-2H-1-benzopyran-7-yl) methanesulfonamide hydrochloride (118 mg, 0.34 mmol), cyclohexyl acetaldehyde (63 mg, 0.50 mmol) and triethylamine (0.034 mL, 0.34 mmol) in methanol (2.4 mL), sodium cyanoborohydride (42 mg, 0.67 mmol) was added at room temperature and the mixture was stirred at the temperature for 2 hours. Upon the completion of the reaction, water was added to the reaction solution, and the resulting solution was extracted with ethyl acetate. The organic phase was washed with saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 1/2) and the aimed product was obtained as oily substance. A solution ~~(0.40 mL, 2.0 mmol)~~ of 4 mol/L hydrogen ~~chloride 1~~chloride in 1,4-dioxane (0.40 mL, 2.0 mmol) was added to the oily substance as 1,4-dioxane solution (0.40 mL), and the resulting mixture was stirred at 0 °C for 30 minutes. Further, di-isopropyl ether (5 mL) was added and the resulting mixture was stirred for 30 minutes, and the resulting crystals were filtered off, and thereby hydrochloride of the aimed product was obtained as colorless solid (yield: 34%).

Please replace the paragraph beginning on page 99, line 27, with the following rewritten paragraph:

Synthesis Example 5

N-{(*3R*, 4S**)-3-~~hydroxy~~Hydroxy-6-methoxy-2,2-dimethyl-4-(n-pentylamino)-3,4-dihydro-2H-1-benzopyran-7-yl} methanesulfonamide

Please replace the paragraph beginning on page 100, line 6, with the following rewritten paragraph:

Synthesis Example 6

N-{(*3R**, *4S**)-3-~~hydroxy~~Hydroxy-2,2,8-trimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-7-yl} methanesulfonamide

Please replace the paragraph beginning on page 100, line 14, with the following rewritten paragraph:

2,2,8-~~trimethyl~~Trimethyl-7-nitro-2H-1-benzopyran

Please replace the paragraph beginning on page 100, line 24, with the following rewritten paragraph:

(*3R**, *4R**)-3,4-~~epoxy~~Epoxy-2,2,8-trimethyl-7-nitro-3,4-dihydro-2H-1-benzopyran

Please replace the paragraph beginning on page 101, line 13, with the following rewritten paragraph:

(*3R**, *4S**)-2,2,8-~~trimethyl~~Trimethyl-7-nitro-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-3-ol

Please replace the paragraph beginning on page 101, line 20, with the following rewritten paragraph:

To a solution of (*3R**, *4R**)-3,4-epoxy-2,2,8-trimethyl-7-nitro-3,4-dihydro-2H-1-benzopyran (600 mg, 2.55 mmol) in 1,4-dioxane (1.2 mL), lithium perchlorate (271 mg, 2.55 mmol) and ~~4-(phenylethyl)amine~~2-(phenylethyl)amine (0.384 mL, 3.06 mmol) were added at room temperature and the mixture was stirred at 80 °C for 1 hour. Upon the completion of the reaction, saturated ammonium chloride was added to the reaction solution, and the resulting solution was extracted with ethyl acetate. The organic phase was washed with saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 4/1) and the aimed product was obtained as orange oily substance (yield: 99%).

Please replace the paragraph beginning on page 102, line 6, with the following rewritten paragraph:

To a solution of (*3R**, *4S**)-2,2,8-trimethyl-7-nitro-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-3-ol (896 mg, 2.51 mmol) and di-t-butyl di-carbonate (1.10 g, 5.03 mmol) in tetrahydrofuran (9.0 mL), triethylamine (700 μL~~mL~~, 5.03 mmol) was added at 0 °C and the mixture was stirred at room temperature overnight. Upon the completion of the reaction, saturated sodium carbonate aqueous solution was added to the reaction solution, and the resulting solution was extracted with ethyl acetate. The organic phase was washed with 1 mol/L hydrochloric acid aqueous solution and saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. After distilling off the solvent, the residue was purified by column chromatography (hexane/ethyl acetate = 4/1) and the aimed product was obtained as colorless amorphous substance (yield: 86%).

Please replace the paragraph beginning on page 104, line 6, with the following rewritten paragraph:

Synthesis Example 7

N-{(*3R**, *4S**)-3-~~hydroxy~~Hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-7-yl} methanesulfonamide maleate

t-Butyl (2-phenylethyl) (*3R**, *4S**)-3-hydroxy-2,2-dimethyl-7-amino-3,4-dihydro-2H-1-benzopyran-4-yl carbamate

Please replace the paragraph beginning on page 104, line 16, with the following rewritten paragraph:

A suspension of (*3R**, *4S**)-2,2-dimethyl-7-nitro-4-[(2-phenylethyl)amino]-2H-1-benzopyran-3-ol maleate (5.20 g, 11.3 mmol) in ethyl acetate was neutralized with an aqueous solution of saturated sodium hydrogen carbonate. The organic phase was washed with saturated sodium chloride solution, and dried over magnesium sulfate. After concentrating under a reduced pressure, the resulting (*3R**, *4S**)-2, 2-dimethyl-7-nitro-4-[(2-phenylethyl)amino]-2H-1-benzopyran-3-ol was diluted with tetrahydrofuran (50 mL). ~~t-Butoxycarbonyl anhydride~~Di-t-butyl dicarbonate (2.96 g, 27.1 mmol) was added thereto and the resulting reaction solution was stirred at room temperature for 1 day and concentrated under a reduced pressure. Ethyl acetate was added to the resulting residue, the resulting mixture was washed with water and saturated sodium chloride solution. The organic phase was dried over magnesium sulfate and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane:ethyl acetate = 10:1) to obtain t-butyl (2-phenylethyl) (*3R**, *4S**)-3-hydroxy-2,2-dimethyl-7-nitro-3,4-dihydro-2H-1-benzopyran-4-yl carbamate (yield: 91%).

Please replace the paragraph beginning on page 104, line 34, with the following rewritten paragraph:

t-Butyl (2-phenylethyl) (*3R**, *4S**)-7-amino-3-hydroxy-2,2-dimethyl-3,4-dihydro-2H-1-benzopyran-4-yl carbamate

Please replace the paragraph beginning on page 105, line 6, with the following rewritten paragraph:

To a solution of t-butyl (2-phenylethyl) (*3R**, *4S**)-3-hydroxy-2, 2-dimethyl-7-nitro-3,4-dihydro-2H-1-benzopyran-4-yl carbamate (4.55 g, 10.3 mmol) in ethanol (91 mL), palladium-carbon (230 mg) was added, and hydrogen was added under normal pressure, and then the mixture was stirred at room temperature for 1 day. The reaction solution was filtered through celite, and the filtrate was concentrated under a reduced pressure. The resulting residue was purified by column chromatography (hexane/ethyl acetate = 5/1) to obtain t-butyl (2-phenylethyl) (*3R**, *4S**)-7-amino-3-hydroxy-2,2-dimethyl-3,4-dihydro-2H-1-benzopyran-4-yl carbamate (yield: 93%).

MS (ESI^+) m / z; 413 [M^++1]
MS (ESI^-) m / z; 457 [M^++45, HCO_2H adduct]

Please replace the paragraph beginning on page 106, line 13, with the following rewritten paragraph:

A solution (24 mL) of 4 mol/L hydrochloric acid-dioxane containing t-butyl (2-phenylethyl) {(*3R**, *4S**)-3-hydroxy-2,2-dimethyl-7-[(methanesulfonyl)amino]-3,4-dihydro-2H-1-benzopyran-4-yl} carbamate (1.2 g, 2.4 mmol) was stirred at room temperature for 1 hour. Ethyl acetate was added to the reaction solution, the reaction solution was washed with 1 mol/L sodium hydroxide aqueous solution and saturated sodium chloride solution. The organic phase was dried over magnesium sulfate and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane:ethyl acetate = 1:1) to obtain N-{(*3R**, *4S**)-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-7-yl} methanesulfonamide (yield: 58%).

Please replace the paragraph beginning on page 106, line 24, with the following rewritten paragraph:

N-{(*3R**, *4S**)-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-7-yl} methanesulfonamide maleate

Please replace the paragraph beginning on page 106, line 31, with the following rewritten paragraph:

To a solution of N-{(*3R**, *4S**)-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-7-yl} methanesulfonamide (66.8 mg, 0.171 mmol) in ethanol, a solution of maleic acid (22 mg, 0.19 mmol) in ethanol was added dropwise. After concentrating under a reduced pressure, the resulting solid was suspended in ethyl acetate. The suspension was stirred and solid was filtered off. The solid was washed with ethyl acetate, dried and thus N-{(*3R**, *4S**)-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-7-yl}-methanesulfonamide maleate (yield: 85%) was obtained.

Please replace the paragraph beginning on page 107, line 11, with the following rewritten paragraph:

Synthesis Example 8

N-{(*3R**, *4S**)-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-1-benzopyran-7-yl} ethanesulfonamide hydrochloride

t-Butyl (2-phenylethyl) (*3R**, *4S**)-7-amino-3-hydroxy-2,2-dimethyl-3,4-dihydro-2H-1-benzopyran-4-yl carbamate

Please replace the paragraph beginning on page 108, line 18, with the following rewritten paragraph:

t-Butyl (2-phenylethyl) (*3R*, 4S**)-7-[(ethylsulfonyl)amino]-3-hydroxy-2,2-dimethyl-3,4-dihydro-2H-benzopyran-4-yl carbamate (239 mg, 0.473 mmol) was suspended in 4 mol/L ~~hydrochloric acid~~ hydrogen chloride in dioxane solution (4mL), and the resulting suspension was stirred at room temperature for 1.5 hour, then solid was filtered off. The solid was washed with ethyl acetate to obtain N-{(*3R*, 4S**)-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-benzopyran-7-yl}-ethanesulfonamide hydrochloride (yield: 66%).

Please replace the paragraph beginning on page 110, line 15, with the following rewritten paragraph:

To a solution of t-butyl (2-phenylethyl) (*3R*, 4S**)-7-amino-3-hydroxy-2,2-dimethyl-3,4-dihydro-2H-benzopyran-4-yl carbamate (1.04 g, 2.52 mmol) in dichloromethane (20 mL), triethylamine (879 μL, 6.30 mmol) was added, and ~~trifluoromethane sulfonyl~~ trifluoromethanesulfonyl chloride (424 μL, 2.52 mmol) was added dropwise at -78°C. After stirring for 1 hour, the resulting mixture was quenched with saturated sodium hydrogen carbonate aqueous solution, heated to room temperature and stirred. Ethyl acetate was added to the reaction solution, the solution was washed with saturated sodium hydrogen carbonate aqueous solution and saturated sodium chloride solution, thereafter the organic phase was dried over magnesium sulfate and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane:ethyl acetate = 2:1) to obtain t-butyl (2-phenylethyl) (*3R*, 4S**)-3-hydroxy-2,2-dimethyl-7-{(trifluoromethyl)sulfonylamino}-3,4-dihydro-2H-benzopyran-4-yl carbamate (yield: 33%).

Please replace the paragraph beginning on page 111, line 6, with the following rewritten paragraph:

A solution of t-butyl (2-phenylethyl) (*3R*, 4S**)-3-hydroxy-2,2-dimethyl-7-{(trifluoromethyl)sulfonylamino}-3,4-dihydro-2H-benzopyran-4-yl carbamate (459 mg, 0.844 mmol) in 4 mol/L ~~hydrochloric acid~~ hydrogen chloride in dioxane (9 mL) was stirred at room temperature. Ethyl acetate was added to the reaction solution, and the solution was washed with 1 mol/L sodium hydroxide aqueous solution and saturated sodium chloride solution. After drying the organic phase on magnesium sulfate, it was concentrated under a reduced pressure to obtain 1,1,1-trifluoro-N-{(*3R*, 4S**)-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl) amino]-3,4-dihydro-2H-benzopyran-7-yl}- methanesulfonamide (yield: 91%) as colorless syrup.

Please replace the paragraph beginning on page 113, line 24, with the following rewritten paragraph:

t-Butyl (2-phenylethyl) (*3R*, 4S**)-3-hydroxy-2,2-dimethyl-7-[N-methyl-N-(methylsulfonyl)amino]-3,4-dihydro-2H-benzopyran-4-yl carbamate

Please replace the paragraph beginning on page 114, line 10, with the following rewritten paragraph:

N-{(*3R*, 4S**)-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-benzopyran-7-yl}-N-methyl-N-methanesulfonamide hydrochloride

Please replace the paragraph beginning on page 114, line 18, with the following rewritten paragraph:

4 mol/L hydrochloric acid-dioxane solution containing t-butyl (2-phenylethyl) (*3R**, *4S**)-3-hydroxy-2,2-dimethyl-7-[N-methyl-N-(methylsulfonyl)amino]-3,4-dihydro-2H-benzopyran-4-yl carbamate (418 mg, 0.828 mmol) was stirred at room temperature for 1.5 hour, then solid was filtered off. The solid was washed with ethyl acetate to obtain N-{(*3R**, *4S**)-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)- amino]-3,4-dihydro-2H-benzopyran-7-yl}-N-methyl-N-methanesulfonamide hydrochloride (yield: 75%).

Please replace the paragraph beginning on page 114, line 31, with the following rewritten paragraph:

Synthesis Example 13

N-{(*3R**, *4S**)-6-bromo-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-benzopyran-7-yl} methanesulfonamide

(*3R**, *4S**)-6-bromo-2,2-dimethyl-7-nitro-4-[(2-phenylethyl)amino] benzopyran-3-ol ~~maleate~~

Please replace the paragraph beginning on page 117, line 33, with the following rewritten paragraph:

t-Butyl (2-phenylethyl) (*3R*, 4S**)-3-hydroxy-2,2-dimethyl-7-dimethylamino-3,4-dihydro-2H-chromen-4-yl carbamate (79.5 mg, 0.175 mmol) was dissolved in 4 mol/L ~~hydrochloric acid~~ hydrogen chloride in dioxane (1.6 mL) solution, and the resulting solution was stirred at room temperature. The resulting solid was filtered off, washed with ethyl acetate and then dried to quantitatively obtain (*3R*, 4S**)-2,2-dimethyl-7-dimethylamino-4-[(2-phenylethyl)amino]-3-chromanol hydrochloride.

Please replace the paragraph beginning on page 119, line 10, with the following rewritten paragraph:

t-Butyl (2-phenylethyl) (*3R*, 4S**)-3-hydroxy-2,2-dimethyl-7-methylamino-3,4-dihydro-2H-chromen-4-yl carbamate (41.5 mg, 0.0973 mmol) was dissolved in 4 mol/L ~~hydrochloric acid~~ hydrogen chloride in dioxane (1.5 mL), some drops of methanol was added thereto and the resulting solution was stirred at room temperature. The resulting solid was filtered off, washed with ethyl acetate and then dried to quantitatively obtain (*3R*, 4S**)-2,2-dimethyl-7-methylamino-4-[(2-phenylethyl)amino]-3-chromanol hydrochloride.

Please replace the paragraph beginning on page 120, line 18, with the following rewritten paragraph:

t-Butyl (*3R**, *4S**)-3-hydroxy-2,2-dimethyl-7-dimethylamino-3,4-dihydro-2H-chromen-4-yl [(2-(4-fluorophenyl)ethyl)] carbamate (72.2 mg, 0.157 mmol) was dissolved in 4 mol/L ~~hydrochloric acid~~ hydrogen chloride in dioxane (2 mL), and the resulting solution was stirred at 50°C. The resulting solid was filtered off, washed with ethyl acetate and then dried to obtain (*3R**, *4S**)-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2-dimethyl-7-dimethylamino-3-chromanol hydrochloride (yield: 97%).

Please replace the paragraph beginning on page 121, line 6, with the following rewritten paragraph:

To a solution of t-butyl (*3R**, *4S**)-7-amino-3-hydroxy-2,2-dimethyl-3,4-dihydro-2H-chromen-4-yl [2-(4-fluorophenyl)ethyl] carbamate (177 mg, 0.412 mmol) in N,N-dimethylformamide (2 mL), potassium carbonate (285 mg, 2.06 mmol) was suspended, methyl iodide (64 μL, 1.0 mmol) was added dropwise to the resulting suspension. After stirring the resulting mixture at 40°C, the reaction solution was diluted with ethyl acetate, and the solution was washed with water and saturated sodium chloride solution. The organic phase was dried over magnesium sulfate and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane:ethyl acetate = 5:1) to obtain t-butyl (*3R**, *4S**)-3-hydroxy-2,2-dimethyl-7-dimethylamino-3,4-dihydro-2H-chromen-4-yl [2-(4-fluorophenyl)ethyl] carbamate (yield: 38%).

Colorless amorphous ~~crystal~~.

Please replace the paragraph beginning on page 121, line 19, with the following rewritten paragraph:

~~Tertiary butyl~~t-Butyl (*3R*, 4S**)-7-amino-3-hydroxy-2,2-dimethyl-3,4-dihydro-2H-chromen-4-yl [2-(4-fluorophenyl)ethyl] carbamate

Please replace the paragraph beginning on page 121, line 26, with the following rewritten paragraph:

To a solution of t-butyl (*3R*, 4S**)-7-amino-3-hydroxy-2,2-dimethyl-3,4-dihydro-2H-chromen-4-yl [2-(4-fluorophenyl)ethyl] carbamate (3.35 g, 7.28 mmol) in methanol (30 mL), palladium/carbon (480 mg) was suspended, hydrogen was added at normal pressure and the resulting solution was stirred at room temperature for 12 hours. The reaction solution was filtered through celite, and the resulting filtrate was concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane:ethyl acetate = 4:1) to obtain t-butyl (*3R*, 4S**)-7-amino-3-hydroxy-2,2-dimethyl-3,4-dihydro-2H-chromen-4-yl [2-(4-fluorophenyl)ethyl] carbamate (yield: 57%).
Colorless amorphous ~~crystal~~.

Please replace the paragraph beginning on page 122, line 2, with the following rewritten paragraph:

t-Butyl (*3R*, 4S**) ~~7-amino~~-3-hydroxy-2,2-dimethyl-3,4-dihydro-7-nitro-2H-chromen-4-yl [2-(4-fluorophenyl)ethyl] carbamate

Please replace the paragraph beginning on page 122, line 9, with the following rewritten paragraph:

To a solution of (*3R**, *4S**)-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2-dimethyl-7-nitro-3-chromanol (3.25 g, 9.02 mmol) in tetrahydrofuran (30 mL), t-butoxycarbonyl anhydride (2.96 g, 27.1 mmol) and triethyl amine (2.5 mL, 18 mmol) were added, and the resulting solution was stirred at room temperature and concentrated under a reduced pressure. The resulting residue was diluted with ethyl acetate, washed with saturated ammonium chloride aqueous solution and saturated sodium chloride solution. Then, the organic phase was dried over magnesium sulfate and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane:ethyl acetate = 4:1) to obtain t-butyl (*3R**, *4S**)-7-~~amino~~nitro-3-hydroxy-2,2-dimethyl-3,4-dihydro-2H-chromen-4-yl [2-(4-fluorophenyl)ethyl] carbamate (yield: 81%).

Please replace the paragraph beginning on page 122, line 22, with the following rewritten paragraph:

(*3R**, *4S**)-4-{[2-(4-~~fluorophenyl~~Fluorophenyl)ethyl]amino}-2,2-dimethyl-7-nitro-3-chromanol

Please replace the paragraph beginning on page 122, line 28, with the following rewritten paragraph:

To a solution of (~~3S~~3R*, ~~4S~~4R*)-3,4-epoxy-2,2-dimethyl-7-nitro-3-chromanol (2.07 g, 9.37 mmol) in dioxane (4 mL), lithium perchlorate (997 mg, 9.37 mmol) and 4-fluorophenethyl-amine (1.47 mL, 11.3 mmol) were added, and the resulting solution was stirred at 70°C for 3.5 hours under nitrogen atmosphere. The reaction solution was diluted with ethyl acetate, washed with saturated sodium hydrogen carbonate solution and saturated sodium chloride solution. Then, the organic phase was dried over magnesium sulfate and concentrated under a reduced pressure. The resulting residue was diluted with ethanol, and a solution of maleic acid (1.20 g, 10.3 mmol) in ethanol was added dropwise thereto. The resulting solid was filtered off, and washed with ethyl acetate. The resulting solid was suspended in ethyl acetate, the resulting suspension was neutralized with 1 mol/L sodium hydroxide aqueous solution and washed with saturated sodium chloride solution. After drying the organic phase over magnesium sulfate, it was dried under a reduced pressure. The resulting rtesidue was purified by silica gel column chromatography (hexane:ethyl acetate = 4:1) to obtain (*3R**, *4S**)-4-{[2-(4-fluorophenyl)ethyl]amino}-2,2-dimethyl-7-nitro-3-chromanol (yield: 81%).

Please replace the paragraph beginning on page 123, line 12, with the following rewritten paragraph:

(*3R**, *4R**)-3,4-~~epoxy~~Epoxy-2,2-dimethyl-7-nitro-3-chromanol

Please replace the paragraph beginning on page 123, line 16, with the following rewritten paragraph:

To a solution of 2,2-dimethyl-7-nitrobenzopyran (11.1 g, 53.9 mmol) in ethyl acetate (165 mL), (Cyc, Ph)-salen manganese complex (XX) (405 mg, 0.431 mmol) and N-methyl imidazole (858 μL, 10.8 mmol) were added, and sodium hypochlorite aqueous solution (101 g, 162 mmol) was added dropwise at 20°C thereto over 15 minutes. After stirring the resulting mixture at room temperature for 3 hours, saturated sodium thiosulfate aqueous solution was added thereto under cooling with water. The resulting reaction solution was filtered through celite, the organic phase was washed with saturated sodium thiosulfate aqueous solution and saturated sodium chloride solution, and then dried over magnesium sulfate, and concentrated under a reduced pressure. The resulting solid was recrystallized in ethanol to obtain (~~*3S*~~*3R**, ~~*4S*~~*4R**)-3,4-epoxy-2,2-dimethyl-7-nitro-3-chromanol (yield: 66%).

Please replace the paragraph beginning on page 123, line 33, with the following rewritten paragraph:

2,2-~~dimethyl~~Dimethyl-7-nitro-1-benzopyran

Please replace the paragraph beginning on page 124, line 4, with the following rewritten paragraph:

To a mixed solution of 6-amino-2,2-dimethyl-7-nitro-1-benzopyran (19.5 g, 88.7 mmol) in methanol-concentrated hydrochloric acid (1:1 v/v, 280 mL) and hypophosphorous acid aqueous solution (100 mL), an aqueous solution of sodium nitrite (12.2 g, 178 mmol) was added dropwise over 30 minutes at -3°C, and the resulting solution was stirred at room temperature until bubbling ceased. The reaction solution was diluted with ethyl acetate, washed with water and saturated sodium chloride solution. The organic phase was dried over magnesium sulfate and then concentrated under a reduced pressure. The resulting solid was recrystallized in methanol to obtain 2,2-dimethyl-7-nitro-1-benzopyran (yield: 61%).

Please replace the paragraph beginning on page 124, line 17, with the following rewritten paragraph:

Synthesis Example 17

(*3R**, *4S**)-6-~~methoxy~~Methoxy-2,2-dimethyl-7-dimethylamino-4-[(2-phenylethyl)amino]-3-chromanol

Please replace the paragraph beginning on page 124, line 26, with the following rewritten paragraph:

t-Butyl (2-phenylethyl) (*3R**, *4S**)-3-hydroxy-6-methoxy-2,2-dimethyl-7-dimethylamino-3,4-dihydro-2H-chromen-4-yl carbamate (133 mg, 0.283 mmol) was dissolved in 4 mol/L ~~hydrochloric acid~~ hydrogen chloride in dioxane (2 mL), some drops of methanol were added thereto, and the resulting solution was stirred at room temperature. The reaction solution was diluted with ethyl acetate, washed with 1 mol/L sodium hydroxide aqueous solution and saturated sodium chloride solution, then the resulting organic phase was dried over magnesium sulfate and concentrated under a reduced pressure to obtain (*3R**, *4S**)-6-methoxy-2,2-dimethyl-7-dimethylamino-4-[(2-phenylethyl)amino]-3-chromanol (yield: 79%).

Please replace the paragraph beginning on page 125, line 17, with the following rewritten paragraph:

To a solution of t-butyl (2-phenylethyl) (*3R**, *4S**)-7-amino-3-hydroxy-6-methoxy-2,2-dimethyl-3,4-dihydro-2H-chromen-4-yl carbamate (1.05 g, 2.37 mmol) in N,N-dimethylformamide (10 mL), potassium carbonate (1.64 mg, 11.8 mmol) was suspended, methyl iodide (368 μL, 5.92 mmol) was added dropwise to the resulting suspension. After stirring the resulting mixture at room temperature for 1 hour, the reaction solution was diluted with ethyl acetate, and the solution was washed with water and saturated sodium chloride solution. The organic phase was dried over magnesium sulfate and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane:ethyl acetate = 4:1) to obtain Compound C (yield: 12%) and Compound D (yield: 10%).

Compound C: Colorless amorphous ~~erystal~~

Compound D: Colorless amorphous ~~erystal~~

Please replace the paragraph beginning on page 125, line 30, with the following rewritten paragraph:

Synthesis Example 18

(*3R**, *4S**)-6-~~methoxy~~Methoxy-2,2-dimethyl-7-methylamino-4-[(2-phenylethyl)amino]-3-chromanol hydrochloride

Please replace the paragraph beginning on page 126, line 18, with the following rewritten paragraph:

Synthesis Example 19

(*3R**, *4S**)-2,2-dimethyl-7-~~methylethylamino~~isopropylamino-4-[(2-phenylethyl)amino]-3-chromanol hydrochloride

Please replace the paragraph beginning on page 126, line 27, with the following rewritten paragraph:

t-Butyl (2-phenylethyl) (*3R**, *4S**)-3-hydroxy-2,2-dimethyl-7-~~methylethylamino~~isopropylamino-3,4-dihydro-2H-chromen-4-yl carbamate (69 mg, 0.15 mmol) was dissolved in 4 mol/L ~~hydrochloric acid~~ hydrogen chloride in dioxane (1 mL), and the resulting solution was stirred at room temperature. The resulting solid was filtered off, washed with ethyl acetate and then dried to quantitatively obtain (*3R**, *4S**)-2,2-dimethyl-7-~~methylethylamino~~isopropylamino-4-[(2-phenylethyl)amino]-3-chromanol hydrochloride.

Please replace the paragraph beginning on page 127, line 6, with the following rewritten paragraph:

t-Butyl (2-phenylethyl) (*3R**, *4S**)-3-hydroxy-2,2-dimethyl-7-~~methylethylamino~~isopropylamino-3,4-dihydro-2H-chromen-4-yl carbamate

Please replace the paragraph beginning on page 127, line 13, with the following rewritten paragraph:

To a solution of t-butyl (2-phenylethyl) (*3R**, *4S**)-7-amino-3-hydroxy-2,2-dimethyl-3,4-dihydro-2H-chromen-4-yl carbamate (176 mg, 0.427 mmol) in N,N-dimethylformamide (2 mL), potassium carbonate (295 mg, 2.13 mmol) was suspended, and isopropyl iodide (56 μL, 0.56 mmol) was added dropwise. After stirring at room temperature, the reaction solution was diluted with ethyl acetate, and washed with water and saturated sodium chloride solution. The organic phase was dried over magnesium sulfate, concentrated under a reduced pressure and the resulting residue was purified by silica gel column chromatography (hexane:ethyl acetate = 5:1) to obtain t-butyl (2-phenylethyl) (*3R**, *4S**)-3-hydroxy-2,2-dimethyl-7-~~methylethylamino~~isopropylamino-3,4-dihydro-2H-chromen-4-yl carbamate (yield: 36%).

Please replace the paragraph beginning on page 127, line 25, with the following rewritten paragraph:

Synthesis Example 20

N-{(*3R**, *4S**)-3-~~hydroxy~~Hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-chromen-7-yl}-N-isopropylmethanesulfonamide hydrochloride

Please replace the paragraph beginning on page 127, line 34, with the following rewritten paragraph:

To a solution of t-butyl (2-phenylethyl) (*3R**, *4S**)-3-hydroxy-2,2-dimethyl-7-[(methylsulfonyl)amino]-3,4-dihydro-2H-chromen-4-yl carbamate (512 mg, 1.04 mmol) in N,N-dimethylformamide (5 mL), potassium carbonate (an excess amount) was suspended, isopropyl iodide (208 μL, 2.09 mmol) was added to the resulting suspension, and the resulting mixture was stirred at room temperature. The reaction solution was diluted in ethyl acetate and water, and then washed with water and saturated sodium chloride solution, thereafter the organic phase was dried over magnesium sulfate and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane:ethyl acetate = 3:1) to obtain amorphous ~~crystal~~ (yield: 94%).

Please replace the paragraph beginning on page 128, line 9, with the following rewritten paragraph:

The resulting amorphous ~~crystal~~ (523 mg, 0.982 mmol) was dissolved in 4N ~~hydrochloric acid~~ hydrogen chloride in dioxane solution and the resulting solution was stirred at room temperature. The reaction solution was concentrated under a reduced pressure, and the resulting solid was filtered off. The solid was washed with ethyl acetate to obtain N-{(*3R**, *4S**)-3-hydroxy-2,2-dimethyl-4-[(2-phenylethyl)amino]-3,4-dihydro-2H-chromen-7-yl}-N-isopropylmethanesulfonamide hydrochloride (yield: 31%).